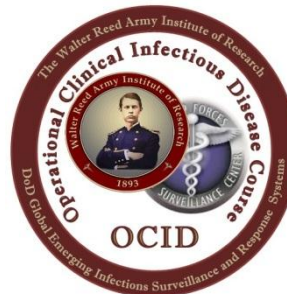


# Leishmaniasis

WRAIR- GEIS 'Operational Clinical Infectious Disease' Course



UNCLASSIFIED

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# Acknowledgments

LTC James E. Moon, MD  
Chief, Sleep Trials Branch  
Walter Reed Army Institute of Research

CDR Ramiro L. Gutierrez, MD  
Chief, Enterics Department  
Naval Medical Research Center

JULY 2015





# Disclaimer

The views expressed in this presentation are those of the speaker and authors, and do not reflect the official policy of the Department of Army, Department of the Navy, Department of Defense, or the U.S. Government



# Leishmaniasis

- Diverse group of diseases caused by infection from protozoan parasites of the genus *Leishmania*
- Designated one of the five most important diseases worldwide by the WHO
  - 1.5 to 2 million new cases/year
- Leishmaniasis threatens over 350 million individuals in 88 countries, and directly impacts US service members abroad

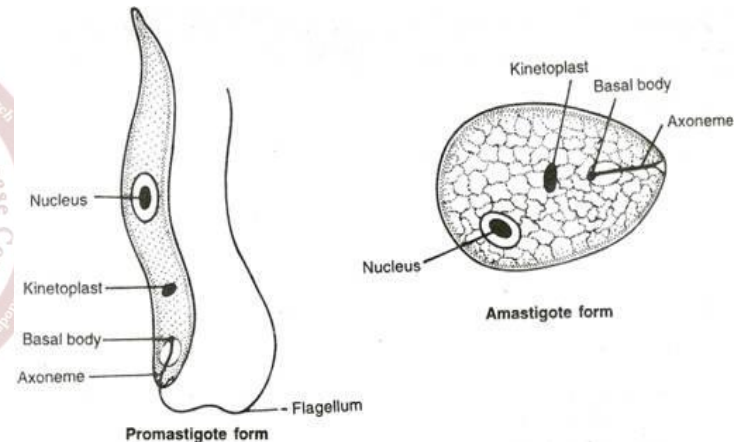


Fig. 178. Morphological forms of *Leishmania donovani*

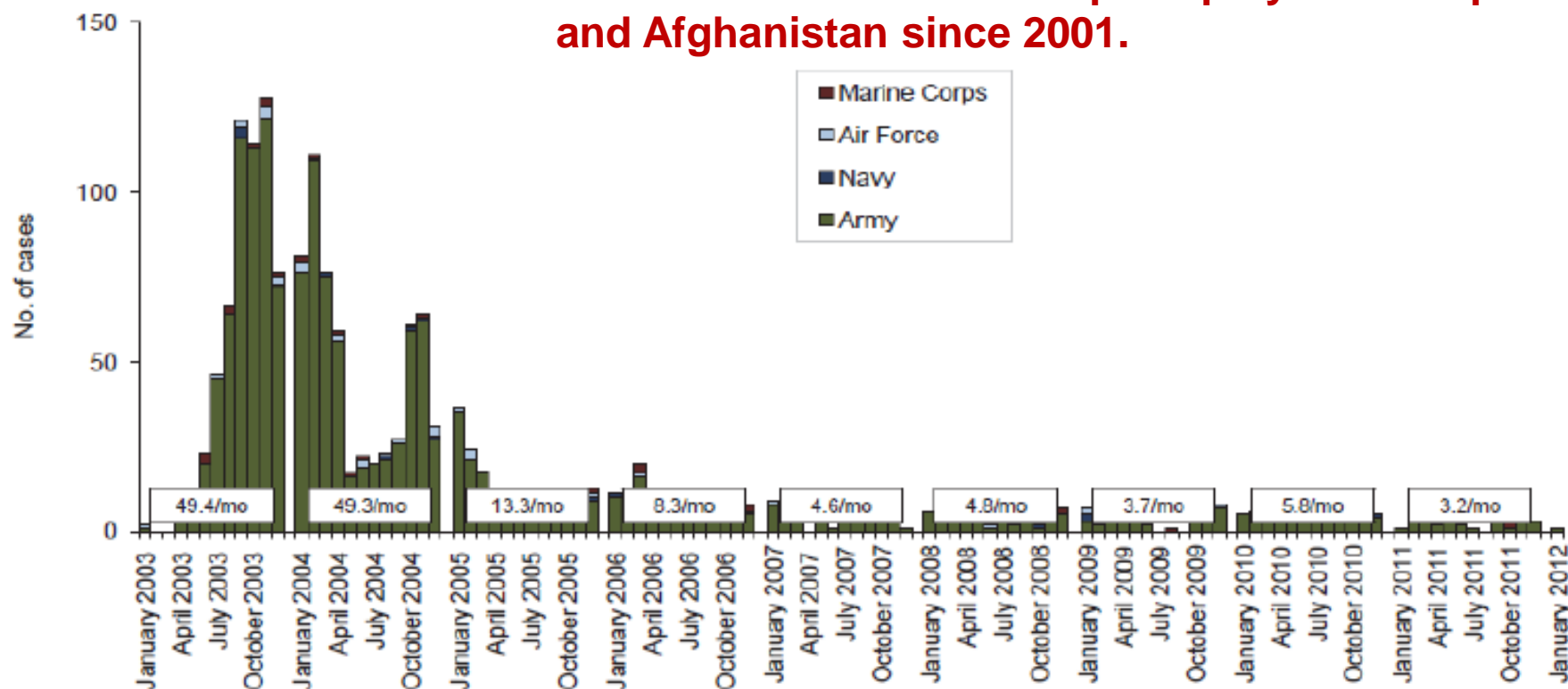
[www.yourarticlelibrary.com](http://www.yourarticlelibrary.com)

# Leishmaniasis among US Armed Forces: 2003-2012



**Over 2000 cases of Leishmaniasis have occurred in American troops deployed to Iraq and Afghanistan since 2001.**

Leishmaniasis (ICD-9: 085.0 to 085.9)<sup>a</sup>



Reference: Army Medical Surveillance Activity. Deployment-related condition of special surveillance interest: leishmaniasis. Leishmaniasis among U.S. Armed Forces, January 2003-November 2004. *MSMR*. Nov/Dec 2004;10(6):2-4.

<sup>a</sup>Indicator diagnosis (one per individual) during a hospitalization, ambulatory visit, and/or from a notifiable medical event during/after service in DEF/OIF/OND.



# *An scourge of many names...*

- Aleppo evil
- Baghdad boil
- Biskra nodule
- Jericho button
- Lahore sore
- pian bois (bush yaws)
- chiclero's ulcer
- uta
- sandfly disease
- espundia
- black fever
- Dum-Dum fever
- kala-azar



Sir William Boog Leishman  
(1865-1926)  
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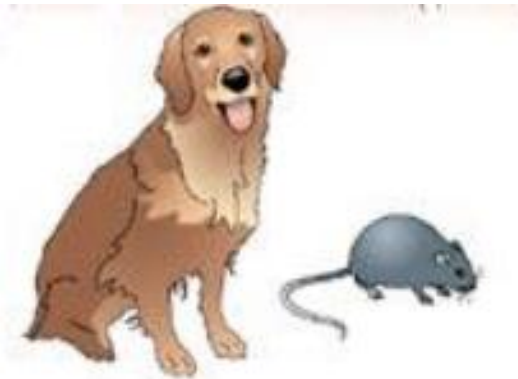
## Vector

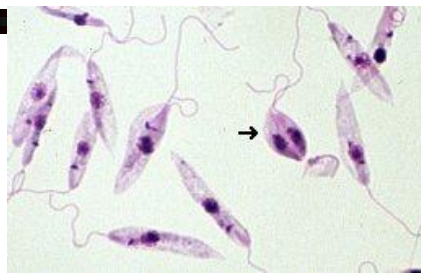
- Female Sand fly
  - *Lutzomyia* in the Americas
  - *Phlebotomus* elsewhere
- Poor flyers, remain near ground
- World wide distribution
- Bites at exposed areas and clothing lines



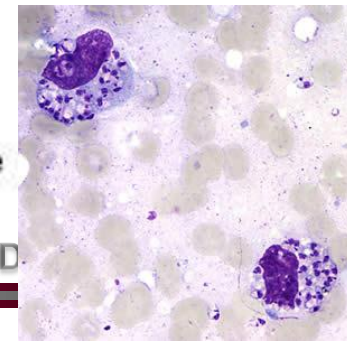
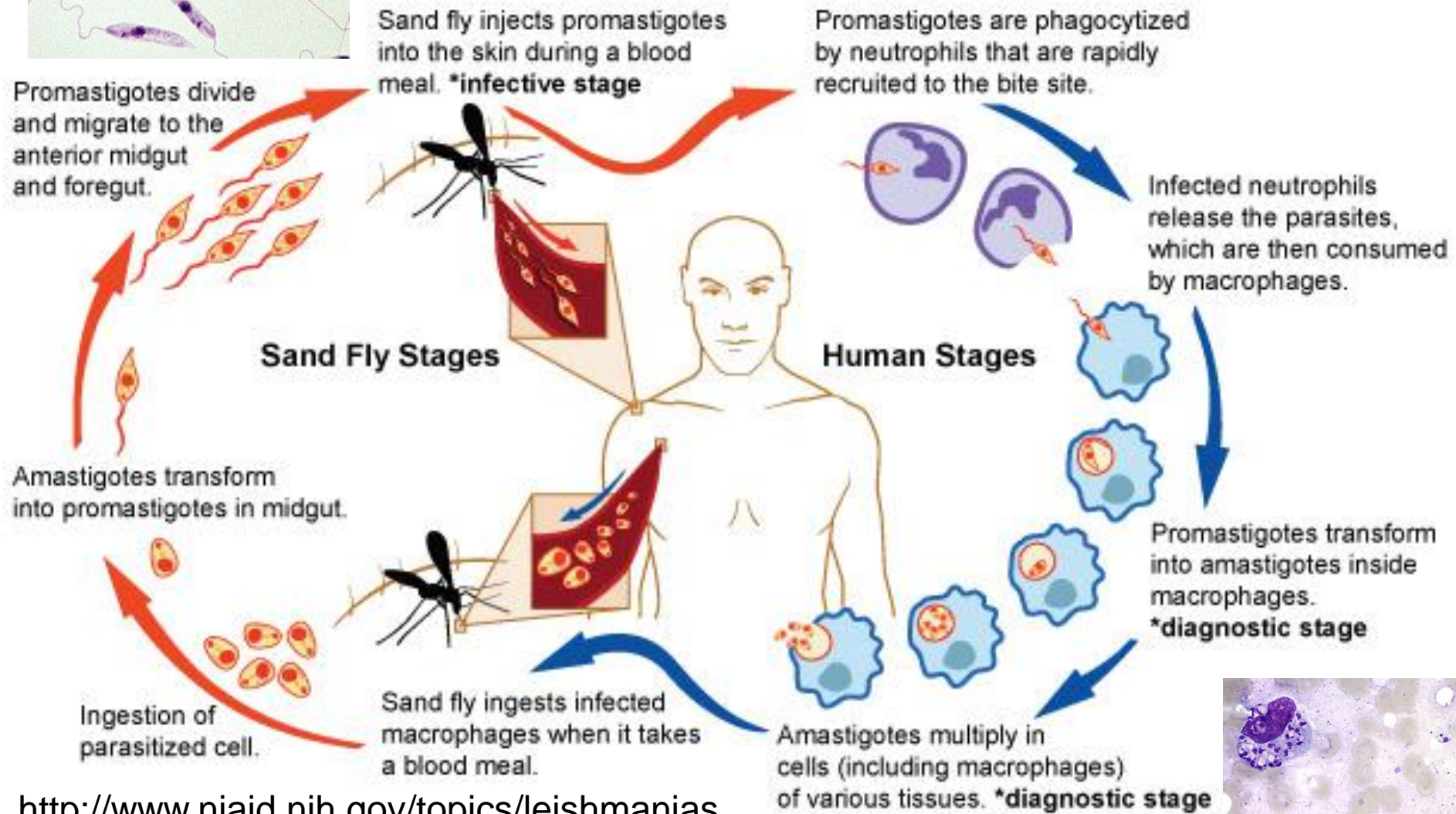
## Reservoirs

- Humans
- Dogs
- Rodents





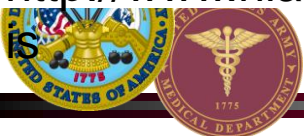
# Transmission\* and Lifecycle



<http://www.niaid.nih.gov/topics/leishmanias>

**\*Also transmitted by blood transfusion!**

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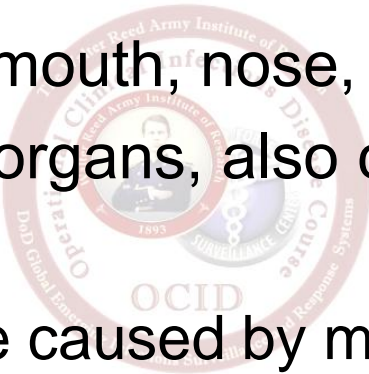




# Disease



- Three clinical syndromes:
  - Cutaneous (skin)
    - Localized, diffuse, *Leishmania recidivans*, post kala-azar dermal leish.
  - Mucocutaneous (mouth, nose, also called “espundia”)
  - Visceral (internal organs, also called “kala-azar”)
- Each syndrome can be caused by multiple different *Leishmania* species, and many species can cause multiple different syndromes
  - Determined by species of parasite, location of infected macrophages, and individual immune response.





# Highly Endemic Areas

- 90% of cutaneous leishmaniasis occur in Afghanistan, Brazil, Iran, Peru, Saudi Arabia, and Syria.
- 90% mucocutaneous leishmaniasis occur in Bolivia, Brazil, and Peru
- 90% of all visceral leishmaniasis cases occur in Bangladesh, Brazil, India, Nepal, and Sudan

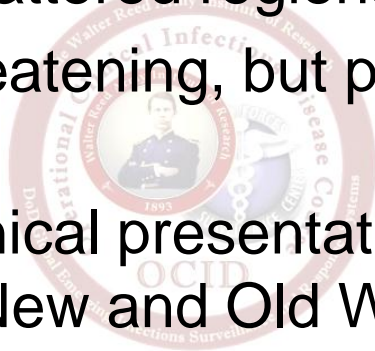
WHO Leishmaniasis: Burden of Disease





# Cutaneous Leishmaniasis (CL)

- Overwhelming majority of Leishmaniasis
  - 1 to 1.5 million cases/year
- Endemic in widely scattered regions throughout the world
- Generally not life-threatening, but potentially permanently disfiguring
- Wide spectrum of clinical presentations that differs somewhat between New and Old World due to regional *Leishmania* species



# Old World Cutaneous Leishmaniasis

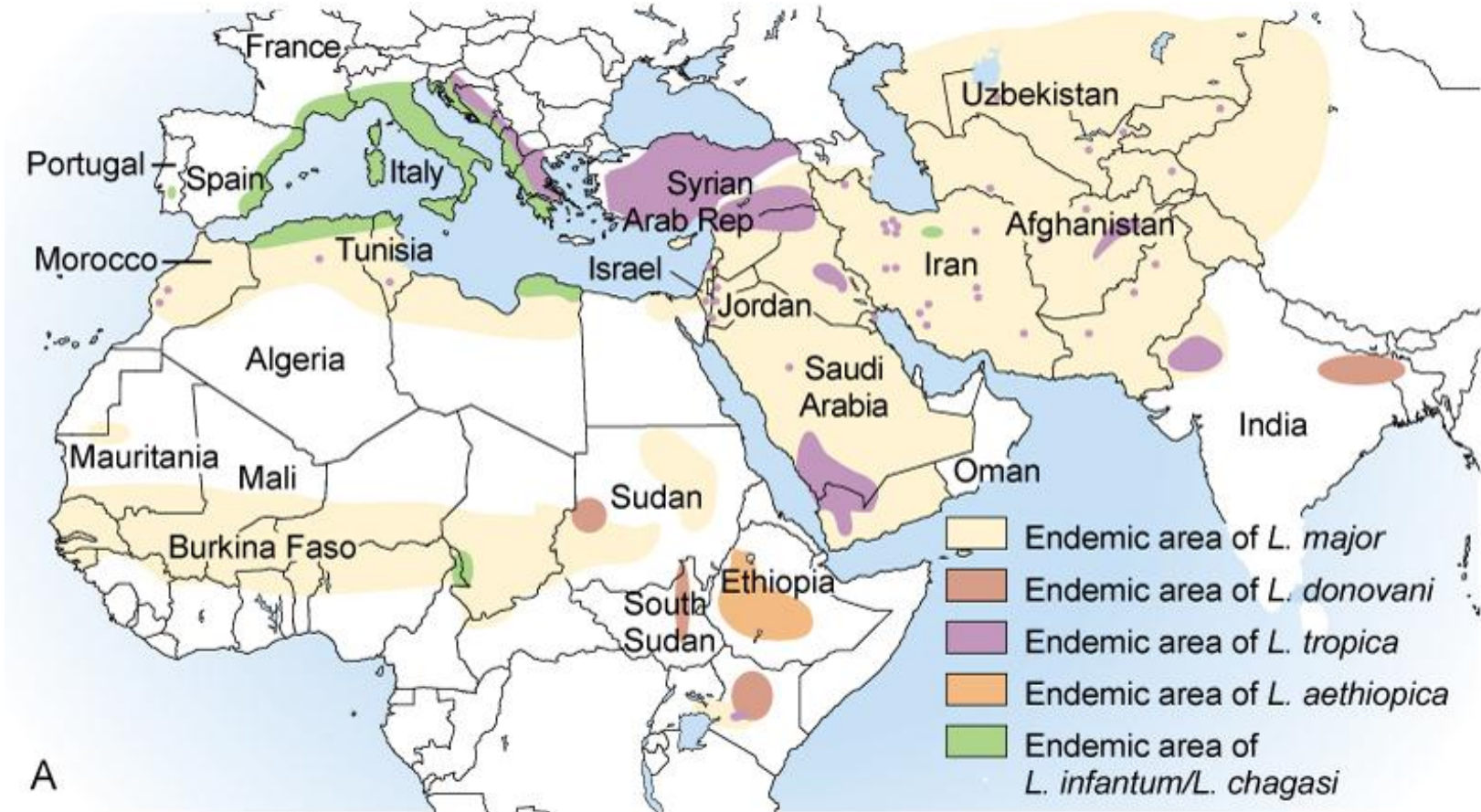


Fig. 277-2A. **Distribution of cutaneous leishmaniasis (CL).** **A**, Old World (Eastern Hemisphere) CL. **B**, New World (Western Hemisphere) CL. Other species causing CL in the New World are not shown but can be found in Table 277-1.

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# New World Cutaneous Leishmaniasis

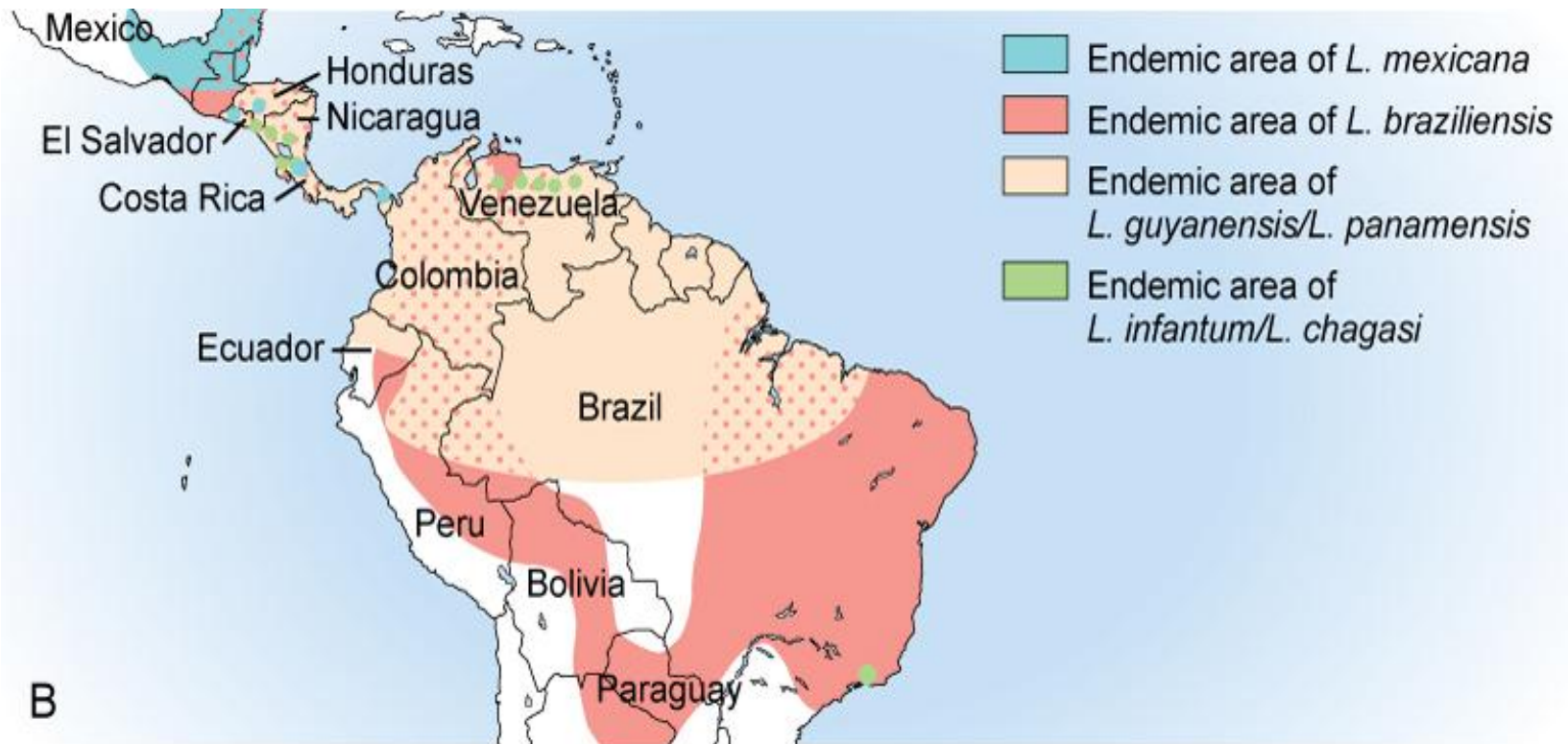


Fig. 277-2B. **Distribution of cutaneous leishmaniasis (CL).** A, Old World (Eastern Hemisphere) CL. B, New World (Western Hemisphere) CL. Other species causing CL in the New World are not shown but can be found in Table 277-1.

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# Common CL Presentations



- New World CL

- Localized disease
- Diffuse disease
- Disseminated disease
- Mucosal disease\*

- Old World CL

- Localized disease
- Diffuse disease
- Post-kala-azar dermal leishmaniasis
- Leishmaniasis recidivans



Fig. 277-10. New World cutaneous leishmaniasis caused by *Leishmania guyanensis*.

\*Mucocutaneous Leishmaniasis (espundia) is considered distinct from CL

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# Localized Cutaneous Leishmaniasis

- Single or multiple lesions, appearance varies
- Nodules develop, expand, ulcerate over weeks
- Incubation time ~ 40 days (days – years)
- **Usually painless or minimally painful**
- Persists months to years, eventually heals with burnlike scar
  - *L. major* most common causative species



“In some cities infection is so common and so inevitable that normal children are expected to have the disease soon after they begin playing outdoors, and visitors seldom escape a sore as a souvenir. Since one attack gives immunity, Oriental sores appearing on an adult person in Baghdad brands him as a new arrival...”

- Chandler A., in “Introduction to Parasitology” 1944



Coleman, et al. J Med Entomol 2006





AUG 9 2002

The Walter Reed Army  
Medical Center  
Clinical Institute



2010/01/27



OCT 24 2003

Photos from Dr. Glenn Wortmann

# Chiclero's Ulcer

- Localized cutaneous leishmaniasis (ear)
- Majority of cases caused by *L. mexicana*
- Chicleros – men who collect the chicle latex from which chiclets chewing gum is made



*Can Med Assoc J* 1986; 134: 216



Photo: Dr. Jason Blaylock

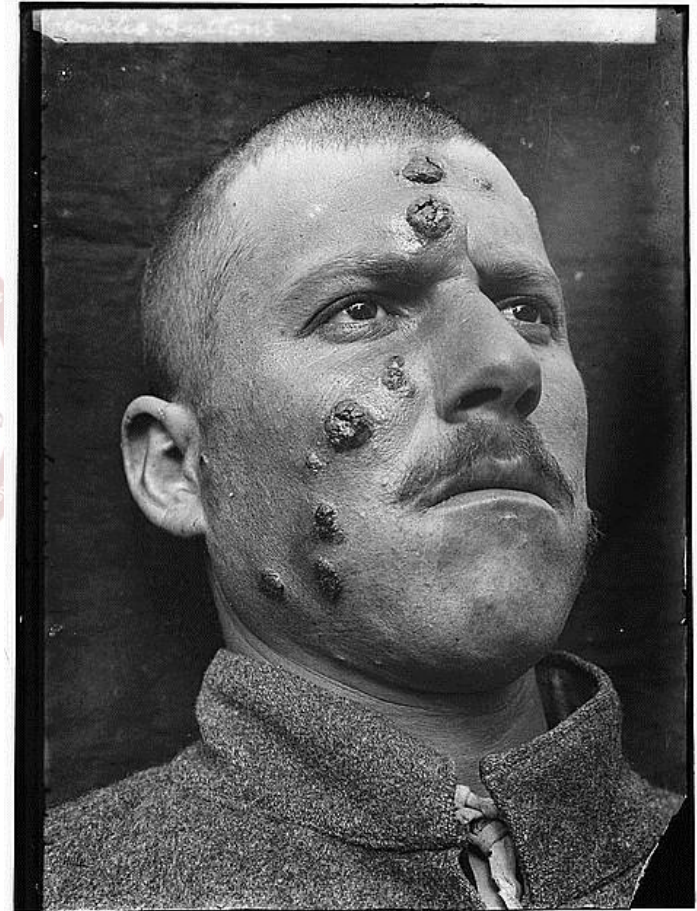




# Diffuse Cutaneous Leishmaniasis

## Jericho Buttons

- Multiple diffuse spreading nodules
  - **Do not ulcerate**
  - Generally face and extremities
- Protracted course-**May be lifelong!**



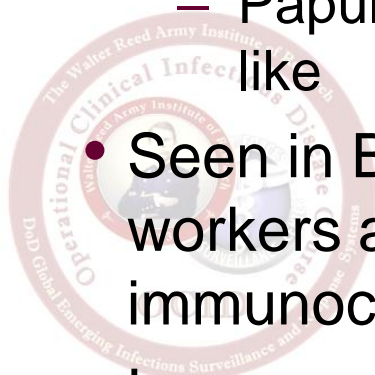
[www.loc.gov](http://www.loc.gov)

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# Disseminated Cutaneous Leishmaniasis



- Characterized by **hundreds of lesions**
  - Papules, nodules, ulcers, acne-like
- Seen in Brazilian agricultural workers and immunocompromised
- Low parasite burden
- May involve mucosa





# Post-kala-azar Dermal Leishmaniasis (PKDL)



- Follows treatment of visceral leishmaniasis
  - up to 4 years later
- Macules progressing to papules, nodules and verrucous (wart-like) forms
  - May resolve or remain chronic (up to 20 years)
  - Can be confused with leprosy



Courtesy Dr. Tom Simpson, Baltimore, MD.

Fig. 277-7. **Post-kala-azar dermal leishmaniasis.** Papular lesions after the treatment of visceral leishmaniasis in Kenya.

PPID, 8<sup>th</sup> ed., pg. 3097

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# PKDL



USUHS teaching slides





# Leishmaniasis recidivans



PPID, 8<sup>th</sup> ed., pg.  
3100



## Leishmaniasis Recidivans Recurrence after 43 Years: A Clinical and Immunologic Report after Successful Treatment

Mary A. Marovich,<sup>1,4</sup> Rosalia Lira,<sup>1</sup> Marc Shepard,<sup>2</sup> Glenn H. Fuchs,<sup>3</sup>  
Richard Kruetzer,<sup>4</sup> Thomas B. Nutman,<sup>1</sup> and Franklin A. Neva<sup>1</sup>

<sup>1</sup>Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland; and Departments of <sup>2</sup>Medicine and <sup>3</sup>Dermatology, George Washington University, and <sup>4</sup>Walter Reed Army Institute of Research, Washington, DC

- Small papules that spread outward leaving a central scar
  - frequently on face
- Chronic
  - waxes and wanes
  - difficult to treat
  - may recur





# Mucocutaneous Leishmaniasis (ML)

- 2-5% of persons with New World CL develop mucous membrane involvement
  - Nose, oral cavity, pharynx, larynx
  - Concurrent or months to **decades** after CL resolves (**can also be primary presentation**)
  - Can be severely mutilating and **life-threatening**







Prof. Luis A. Leon  
LAB. LEON Quito-Ecuador  
Manson-Bahr, 1972



T. Evans © 1996



PPID, 8th ed., pg. 3099



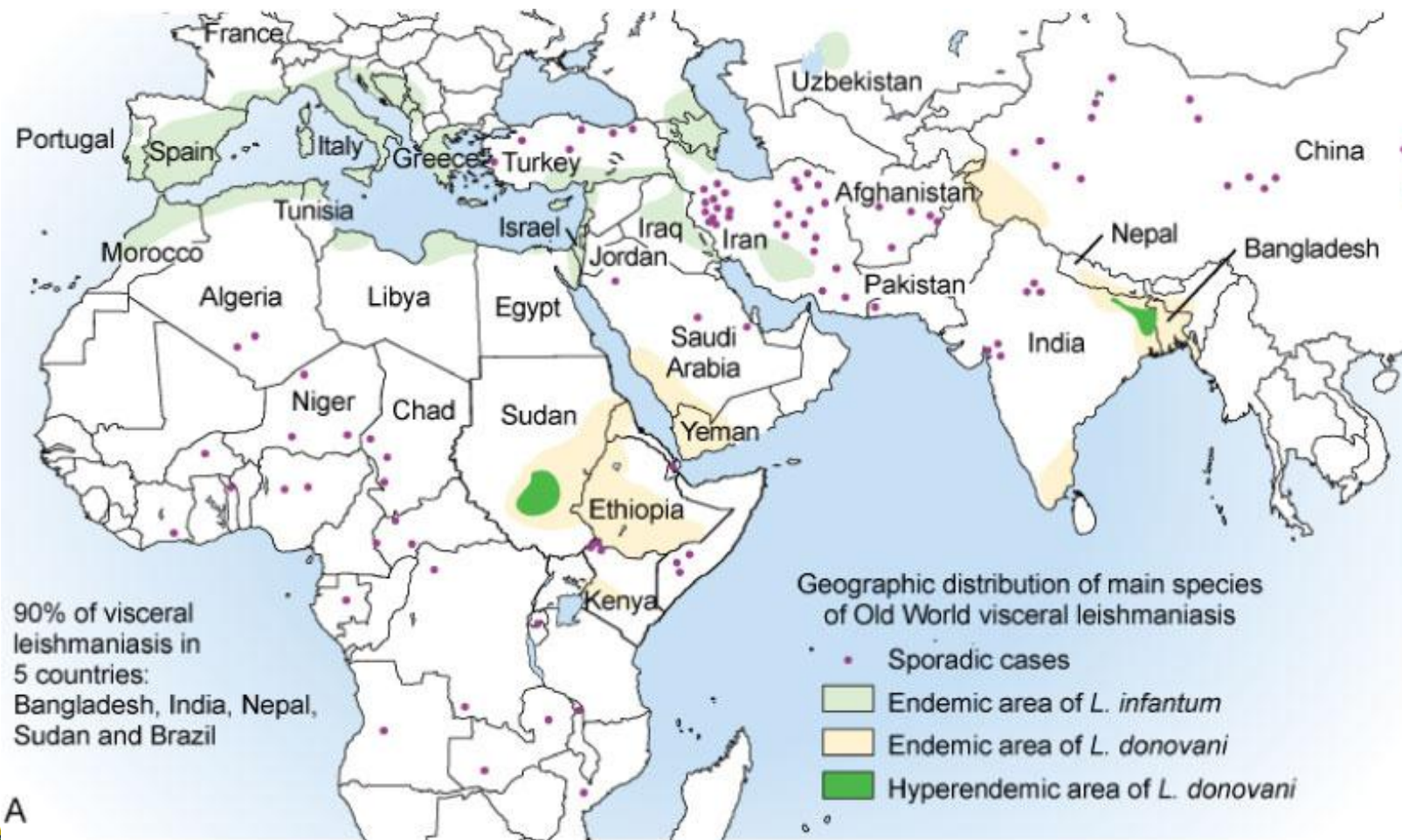


# Visceral Leishmaniasis (VL)

- Leishmanial infection of the internal organs
- Unlike CL, generally similar in all regions
- Incubation: 2-8 months (10 days to >1 year)
- Wide spectrum of presentations
  - majority asymptomatic (6.5-18:1 ratio)
  - asymptomatic to subacute to severe multi-organ disease
  - can spontaneously resolve over weeks to months, or progress to **fatality** if not treated



# Visceral Leishmaniasis in the Old World



A

Fig. 277-3A. Distribution of visceral leishmaniasis (VL). A, Old World (Eastern Hemisphere) VL. B, New World (Western Hemisphere) VL.



# Visceral Leishmaniasis in the New World

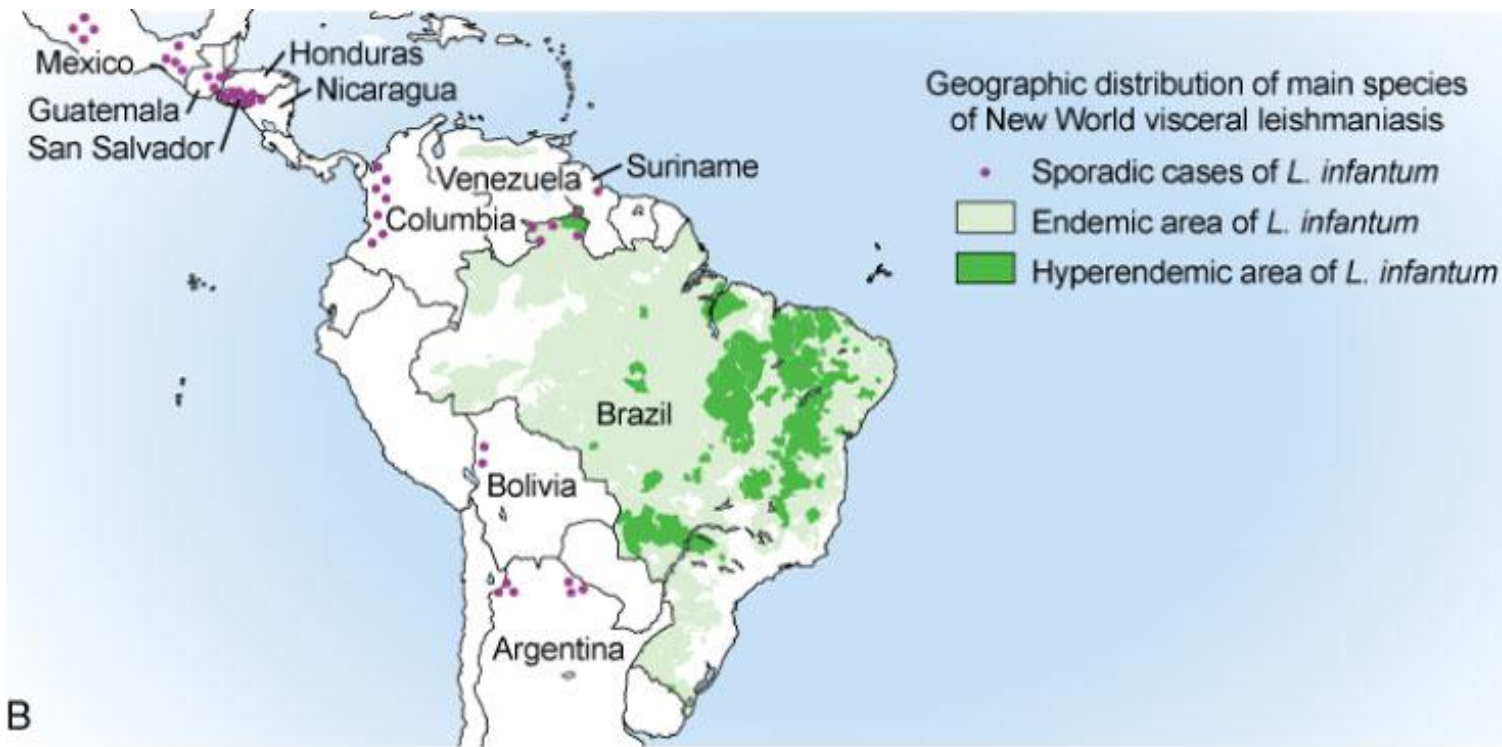


Fig. 277-3B. **Distribution of visceral leishmaniasis (VL).** A, Old World (Eastern Hemisphere) VL. B, New World (Western Hemisphere) VL.

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# kala-azar (black or fatal sickness)

- Severe VL
  - Classic pentad: prolonged fever, weight loss, hepatosplenomegaly, pancytopenia, hypergammaglobulinemia
- Progressive (variable rates)
- > 90% mortality within first two years
- Can be opportunistic infection in immunocompromised state



Courtesy Dr. Charles Oster, Washington, DC.

Fig. 277-6. Children with visceral leishmaniasis in Kenya. Note signs of malnourishment and protruding abdomen with massive hepatomegaly.



# Viscerothropic Leishmaniasis from Desert Storm (*L. tropica*)

- Rare, low-grade, syndrome first identified in 8 patients returning from Operation Desert Storm
  - Fevers: 6 of 8
  - Weight loss: 2 of 8
  - Nausea, vomiting, low-grade watery diarrhea: 2 of 8
  - Lymphadenopathy: 2 of 8
  - Hepatosplenomegaly: 2 of 8
  - Anemia: 3 of 8
  - Leukopenia or thrombocytopenia: 0 of 8
  - Elevated liver enzymes: 6 of 8
  - No symptoms: 1 of 8
- Similar syndromes since found in Brazil and Italy

Magill et al, NEJM 1993;328(19)





# Diagnosis

- Clinical Diagnosis
- Cutaneous Leishmaniasis
  - Biopsy/Aspiration/Scraping
  - Amastigotes in a smear
  - Promastigotes in culture
  - PCR of sample (DNA/RNA)
- Visceral Leishmaniasis
  - Biopsy of Bone Marrow or Spleen
    - Touch Prep, PCR, Culture
  - Immunologic
    - rK39 leish. antigen direct agglutination test







NOV 13 2003



NOV 13 2003



NOV 13 2003



NOV 20 2003



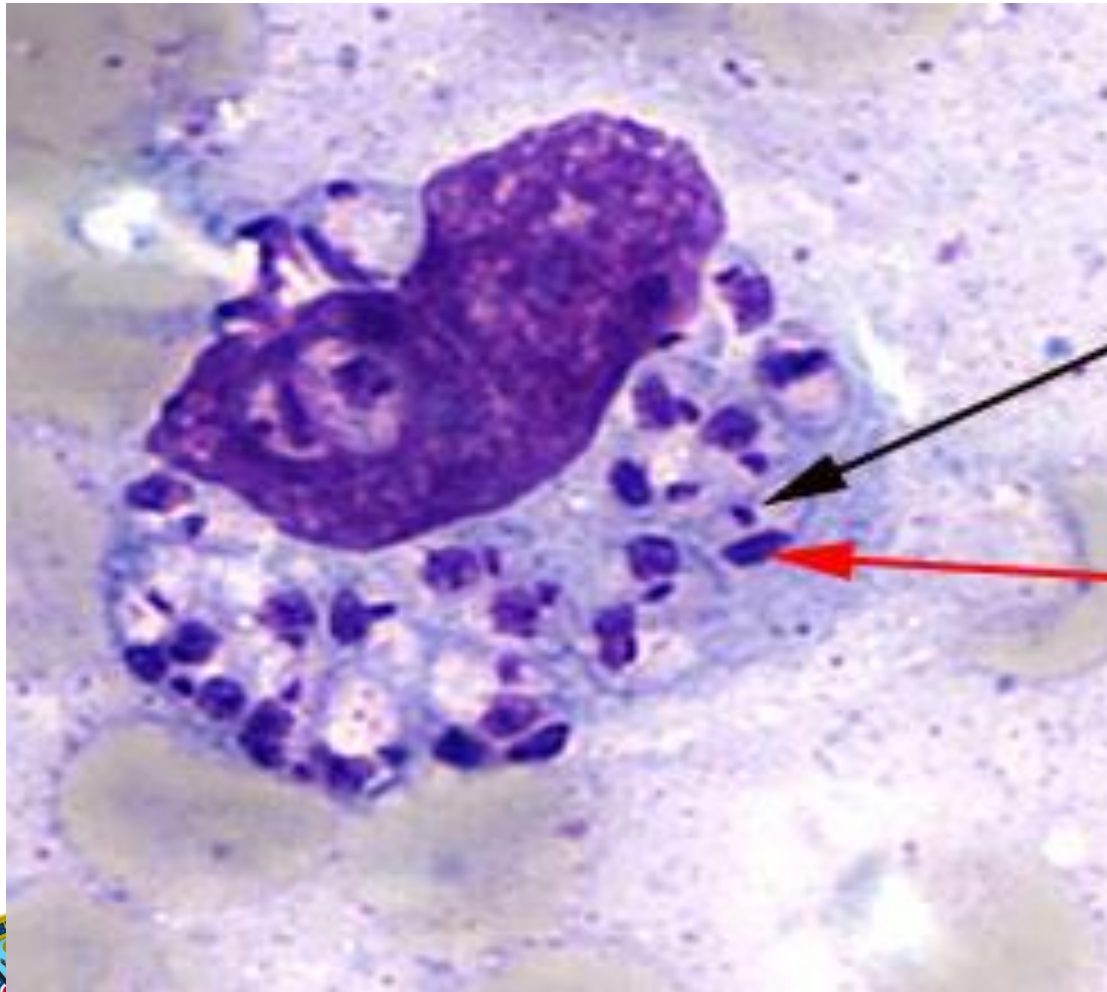
NOV 13 2003



Biopsy should just catch edge of most affected tissue and should have relatively intact tissue adjacent to the lesion for at least one half of biopsy



# Tissue Diagnosis –skin, spleen, bone marrow



- **Infected Macrophage with amastigotes**
  - a nucleus (red arrow)
  - a rod-shaped kinetoplast (black arrow).

Photo: CDC

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# Diagnosis - culture

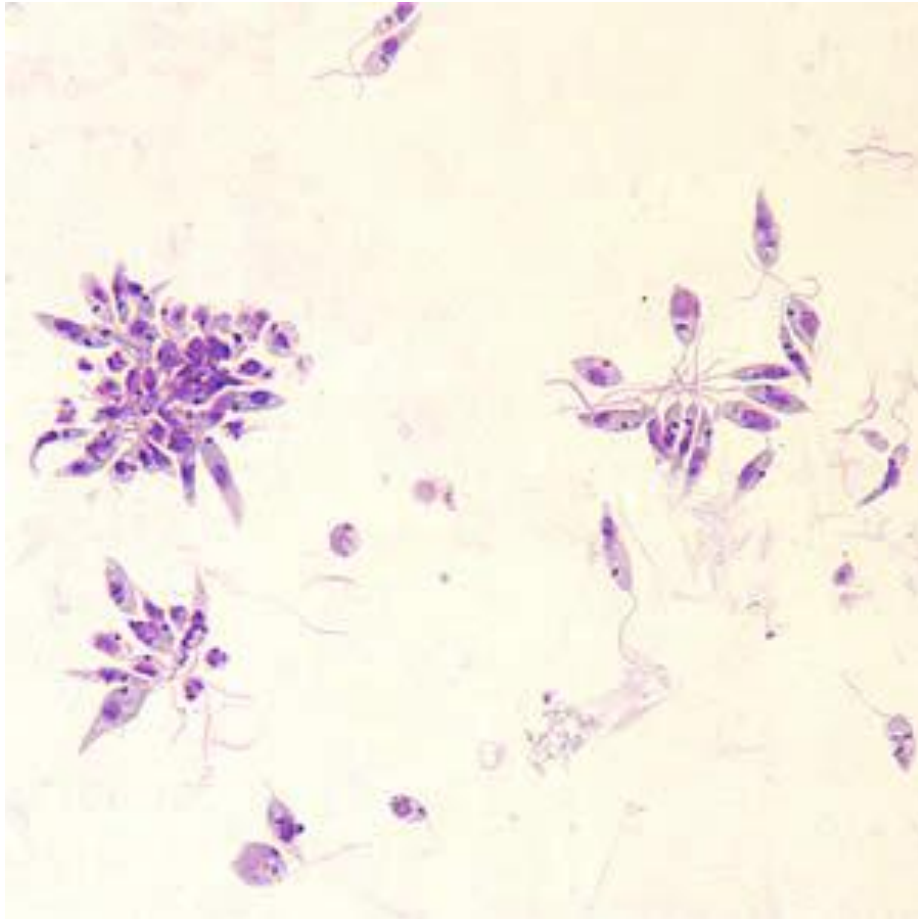


Photo: CDC

## Promastigotes

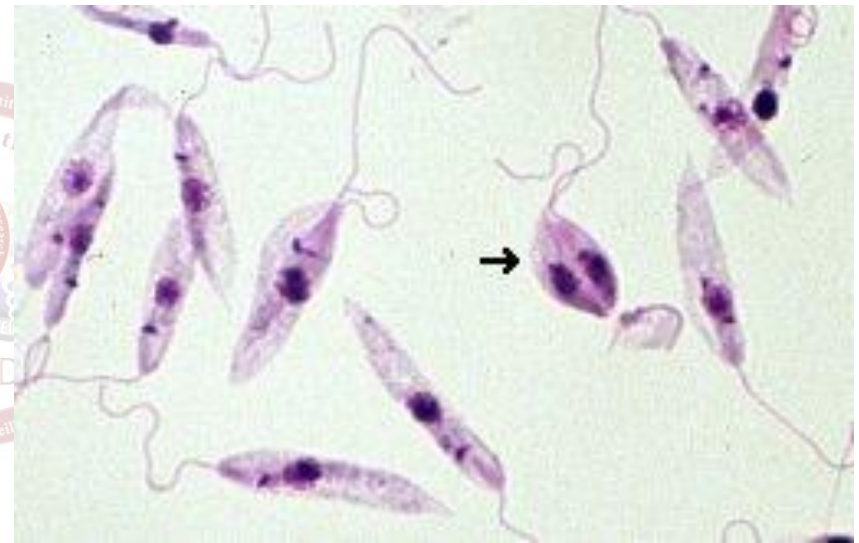


Photo: [www.msu.edu](http://www.msu.edu)

# Diagnosis



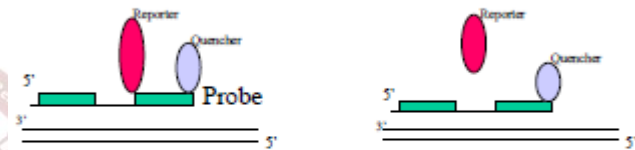
## Montenegro Skin Test

- AKA Leishmanin Test
- Injection of dead promastigotes into skin
  - DTH Reaction (wheal) suggests infection
- Not licensed in U.S

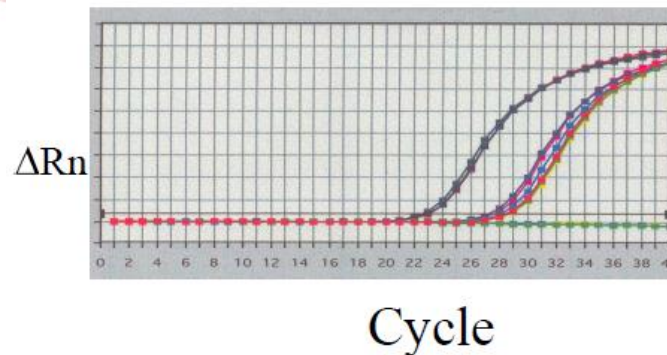


## PCR

### Real-Time PCR



During each extension cycle, the Taq DNA polymerase cleaves the reporter dye from the probe



*L. major*

*L. major*

*L. V. panamensis*

Negative control







*InBios*

**Kalazar Detect**

Lot #: DC1015    Exp: 08/2004

Store at Room Temperature

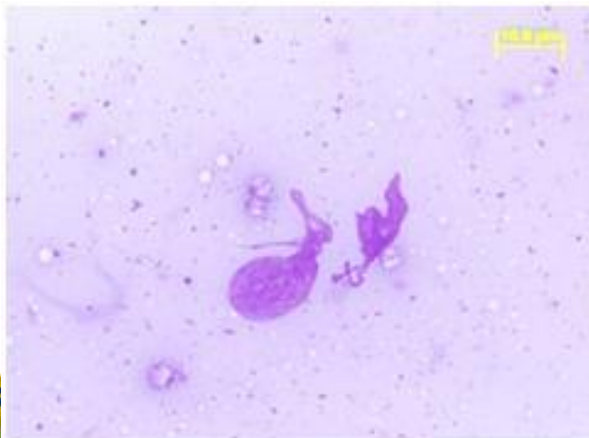
For Research Use Only

Manufactured in the USA by *InBios* International, Inc.  
Seattle, Washington 98104





- **Leishmania Diagnostics Laboratory**
- [http://wrair-www.army.mil/OtherServices\\_LDL.aspx](http://wrair-www.army.mil/OtherServices_LDL.aspx)
- [usarmy.detrick.medcom-wrair.mbx.leishmania-diagnostic@mail.mil](mailto:usarmy.detrick.medcom-wrair.mbx.leishmania-diagnostic@mail.mil)
- Juan Mendez - **240-595-7353**
- **ID or Dermatology Electronic Consult Service**





# Treatment

- Treatment is not standardized
  - What works on one species and clinical presentation may fail in another
  - Must adapt to regional experience
  - Much is anecdotal and off-label
- In general, treatments result in **clinical cure, but not parasitological cure**
  - Lifelong potential for reactivation in immunocompromised





# Treatment Options

- CL
  - Watchful waiting
  - Local destructive therapies
    - Liquid NO<sub>2</sub>
    - Thermo-Med device
  - Topical creams
    - Paromomycin
  - Systemic treatment
    - Amphotericins (Ambisome)
    - Pentavalent Antimonials
      - Sodium stibogluconate (Pentostam)\*
      - Meglumine Antimoniate (Glucantime)
    - Azoles (Fluconazole, Ketoconazole, Itraconazole)
    - Pentamidine
    - Miltefosine (Impavido)\*\*
- ML, VL
  - Systemic treatment
    - Pentavalent Antimonials
      - Sodium stibogluconate (Pentostam)\*
      - Meglumine Antimoniate (Glucantime)
    - Azoles (Fluconazole, Ketoconazole, Itraconazole)
    - Amphotericins (Ambisome)\*\*\*
    - Miltefosine (Impavido)\*\*
    - Paromomycin
  - Alone or in combination



- \* Available in US on IND
- \*\* Only Drug FDA approved for CL in US
- \*\*\* Only drug FDA approved for VL in US





# CL-When to consider doing nothing

CRITERIA	FAVORS NO TREATMENT	TREATMENT USUALLY INDICATED
<b>Age and direction of healing</b>	Clearly improving compared to prior month	Worsening lesions
<b>Number of lesions</b>	One or a few	>5 and in different locations
<b>Complexity</b>	Uncomplicated	Restricts movement or wearing of clothes, cosmetic concerns
<b>Size of lesion(s)</b>	Small (<1 cm)	Very large (>5cm)
<b>Immune status</b>	Immunocompetent	Immunocompromised
<b>Mucosal involvement</b>	None	Yes
<b>Location</b>	Nonexposed skin	Exposed skin, especially facial
<b><i>L. braziliensis</i>?</b>	No or unlikely	Yes or likely*
<b>How bothersome to patient and family?</b>	No or little concern	Very concerned or preoccupied

\*If Bolivia, Brazil, Peru, should be treated with systemic therapy due to risk of mucosal involvement

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# Watchful Waiting

- CL due to *L. major* (MON-26) in Saudi Arabia
  - Healing time (after study enrollment)
    - 6 weeks – 6%
    - 3 months – 34%
    - Alrajhi, *et al.*, NEJM 2002; 346
- CL in Guatemala
  - *L. mexicana* healing/cure – 68% (avg. 14 wks)
  - *L. braziliensis* healing/cure – 6% (avg. 13 wks)
    - Herwaldt, *et al.*, J Infect Dis 1992; 165



# No Treatment

- CL acquired in Afghanistan
- Evaluated in Nov 2008 with 3 cm ulcer
- No treatment
- Follow-up in Jun 2009



Photo courtesy of Dr. Julie Ake



# Locally Destructive Therapies

## LNO<sub>2</sub>

- Freezes lesions to kill parasites
- May cause hypopigmentation
- Not standardized
  - Cryoprobe suggested
- Painful / blister formation

## ThermoMed

- Heats lesions to kill parasites
- ~ 70 % efficacy in CL caused by *L. major* in Iraq and *L. tropica* in Afghanistan



Reithinger, et al CID 2005  
Aronson, et al PloS Negl Trop Dis 2010  
Photo: Dr. Glenn Wortmann





Day 4



Day 6



Day 8



# Topical Cream: Paromomycin



- Aminoglycoside
- Compounded
  - 15% paromomycin
  - +/- 0.5% gentamicin
- Apply to affected area twice a day x 28 days
- 81% cure - *L. major*

[N Engl J Med.](#) 2013 Feb  
7;368(6):524-32



[mrmc.amedd.army.mil](http://mrmc.amedd.army.mil)

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# Systemic Treatment: Miltefosine

- Phosphocholine analogue
- **Oral**
- 28 day regimen
  - 50mg po bid x 28 days
- Used worldwide for all forms of Leishmaniasis
- FDA approved for CL only (2014)
- Side effects:
  - **nausea, vomiting, abdominal pain**
  - LFT abnormalities
  - Increased creatinine
- **Teratogenic –Do not Use in Pregnancy!**



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# Systemic Treatment: Azoles

- Fluconazole
- Ketoconazole, Itraconazole
- Limited data
- Variable regimens
  - Oral
  - 4-6 weeks or longer
  - Weight based
- Variable efficacy

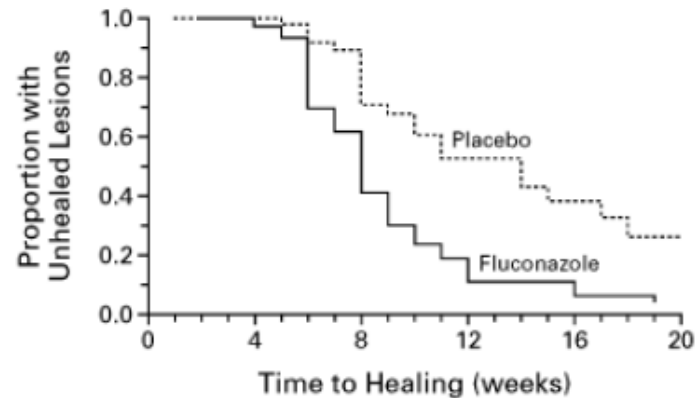






# Fluconazole

- Prospective study
  - 200mg daily for 42 days
- 6 weeks: 29% vs 6% placebo
- 3 months: 79% vs 34% placebo



Alrajhi, et al. NEJM 2002;346:891





# Interventions for Old World cutaneous leishmaniasis (Review)

## Authors' conclusions

Most trials have been designed and reported poorly, resulting in a lack of evidence for potentially beneficial treatments. There is a desperate need for large well conducted studies that evaluate long-term effects of current therapies. We suggest the creation of an international platform to improve quality and standardization of future trials in order to inform clinical practice.

In *Leishmania major* infections, there was good RCT evidence of benefit of cure around 3 months after treatment when compared to placebo for 200 mg oral fluconazole (1 RCT n = 200, RR 2.78; 95% CI 1.86, 4.16), topical 15% paromomycin + 12% methylbenzethonium chloride (PR-MBCL) (1 RCT n = 60, RR 3.09; 95% CI 1.14, 8.37) and photodynamic therapy (1 RCT n = 60, RR 7.02; 95% CI 3.80, 17.55). Topical PR-MBCL was less efficacious than photodynamic therapy (1 RCT n = 65, RR 0.44; 95% CI 0.29, 0.66). Oral pentoxifylline was a good adjuvant therapy to intramuscular meglumine antimoniate (IMMA) when compared to IMMA plus placebo (1 RCT n = 64, RR 1.63; 95% CI 1.11, 2.39)

In *Leishmania tropica* infections, there was good evidence of benefit for the use of 200 mg oral itraconazole for 6 weeks compared with placebo (1 RCT n = 20, RR 7.00; 95% CI 1.04, 46.95), for intralesional sodium stibogluconate (1 RCT n = 292, RR 2.62; 95% CI 1.78, 3.86), and for thermotherapy compared with intramuscular sodium stibogluconate (1 RCT n = 283, RR 2.99; 95% CI 2.04, 4.37).

**This record should be cited as:** González U, Pinart M, Reveiz L, Alvar J. Interventions for Old World cutaneous leishmaniasis. *Cochrane Database of Systematic Reviews* 2008, Issue 4. Art. No.: CD005067. DOI: 10.1002/14651858.CD005067.pub3.





# Systemic Treatment: Antimonials

- Sodium stibogluconate (Pentostam)
  - Investigational New Drug
  - Available from the CDC for civilians
  - Available from Walter Reed for military
  - Regimen
    - CL: intravenous 20mg/kg/day for 10-20 days
      - Outside US is often given intra-lesionally
    - VL: intravenous 20mg/kg/day for 28 days







0302 pre (4/21/03)



0302 post therapy 5/10/03



Photos: Dr. Glenn Wortmann

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The Walter Reed Army Institute of Research  
 Medical Infections  
 Institute of Research  
 1993  
 OCI  
 tions Sur

# Pentostam®

- Toxicities
  - Elevated amylase/lipase ~95%
  - Elevated liver enzymes ~50%
  - Arthralgias/myalgias ~65%
  - Rare significant EKG changes/cytopenias
  - Dermatological ~10%
    - Wide range of presentations
    - Herpes zoster virus (shingles)

**DO NOT USE IN PREGNANCY**

Aronson, et al. Clin Infect Dis 1998;27:1457-64  
Wortmann, et al. Clin Infect Dis 1998;27:509-12  
Wortmann, et al. Clin Infect Dis 2002;35:261-7

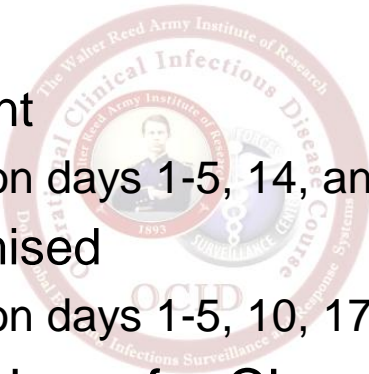






# Systemic Treatment: Amphotericins

- Liposomal Amphotericin B (Ambisome)
  - Drug of choice for VL
  - Regimen (IV)
    - Immunocompetent
      - 3 mg/kg/day on days 1-5, 14, and 21
    - Immunocompromised
      - 4 mg/kg/day on days 1-5, 10, 17, 24, 31, 38
  - No established regimen for CL
  - Extensive side-effect profile



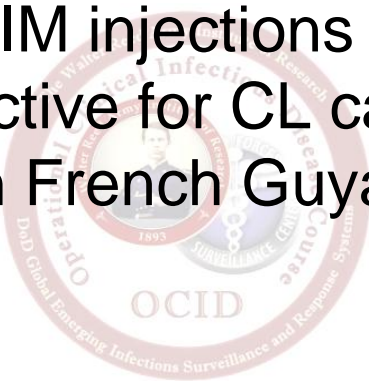


*L. guyanensis*—Fr Guiana—  
Ambisome for 7 doses



# Systemic Treatment: Pentamidine

- No longer recommended for VL due to high toxicity
- One indication only
  - Short course (2 IM injections of 4mg/kg) has been found to be effective for CL caused by *L. guyanensis* in French Guyana and Surinam only





# Systemic Dosing Summary

- Cutaneous Leishmaniasis
  - Pentostam – 20 mg/kg IV x 10 -20 days
  - Ambisome (liposomal amphotericin B)
    - 3 mg/kg on days 1-5, 14, & 21
  - Fluconazole – 8 mg/kg/day (4 – 12 weeks)
  - Miltefosine –50mg po twice a day x 28 days
- Visceral Leishmaniasis
  - Ambisome (liposomal amphotericin B) 3 mg/kg on days 1-5, 14, & 21
  - Pentostam – 20 mg/kg IV x 28 days
  - Miltefosine –50mg po twice a day x 28 days







# Prevention

- Sandflies bite and are active at night (warmer months)
- Stay **indoors** between dusk and dawn
- Keep dogs and susceptible animals indoors at night
- Use fans - sandflies are **poor fliers** deterred by wind
- Sandflies are **small and can get through mesh** netting if not extremely fine
- House **construction** and modification; sandflies breed in cracks of houses
- Insecticides on people and animals
- Help from entomologists
- Dog vaccine available in Brazil





# Sandfly Habitat

(a)



(b)



(c)



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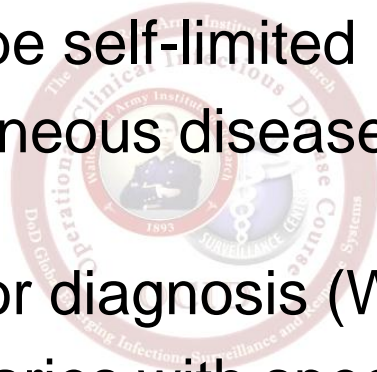


OCID course 2015



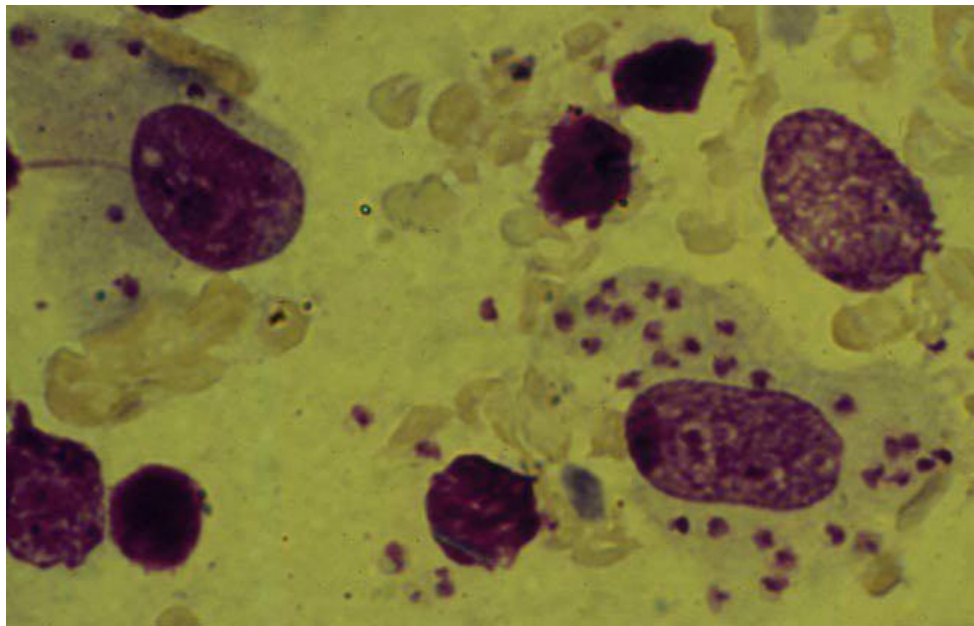
# Summary – Leishmaniasis

- Worldwide distribution
- Many species with different disease presentations
- Cutaneous form may be self-limited
- Think about mucocutaneous disease, especially in South America
- Resources available for diagnosis (WRAIR)
- Treatment response varies with species and host





# Thank You





# Extra Slides



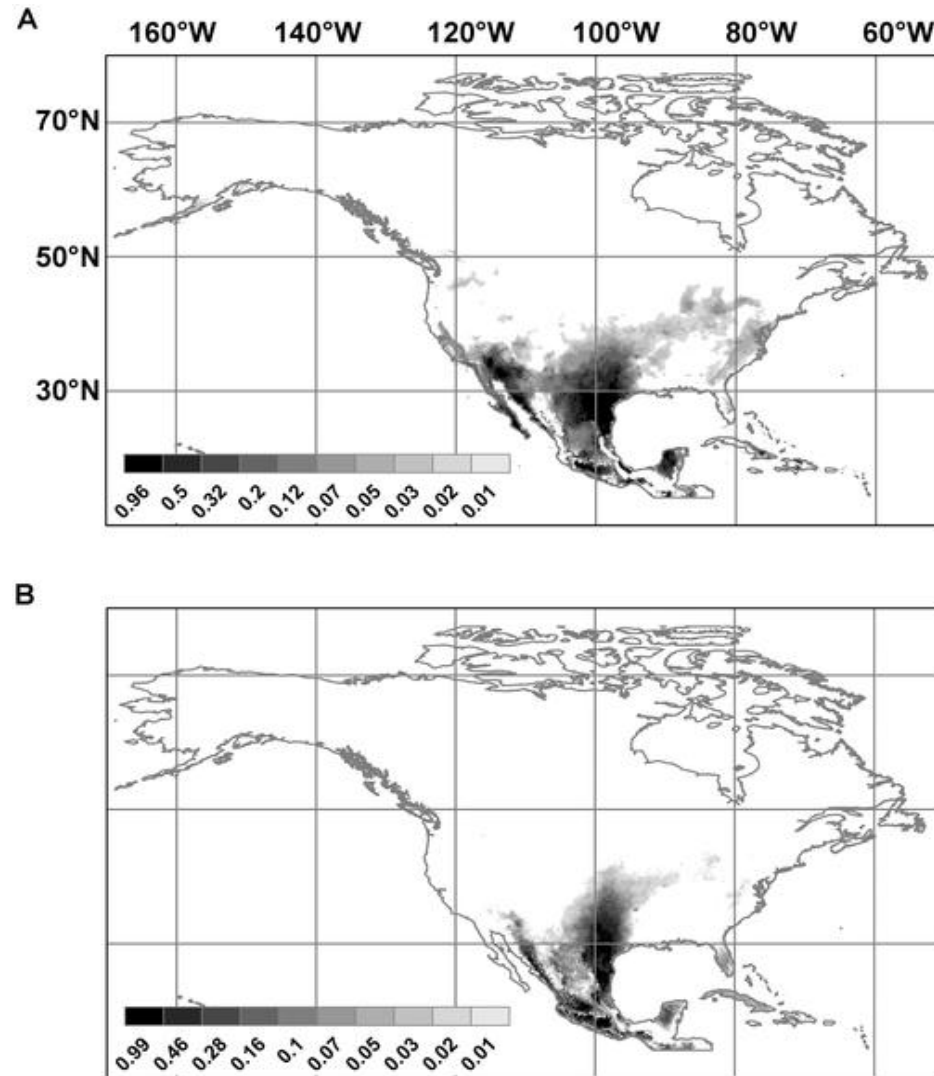


# Classification

- *Old World, Cutaneous Disease:*
  - *L. tropica*; *L. major*, *L. aethiopica*
  - *L. tropica* can cause visceral disease
- *Old World, Visceral Disease:*
  - *L. donovani* complex with 3 species (*L. donovani*, *L. infantum*, and *L. chagasi*)
- *New World, Cutaneous disease:*
  - *L. mexicana* complex with 3 main species (*L. mexicana*, *L. amazonensis*, and *L. venezuelensis*)
- *New World, Cutaneous and Mucocutaneous disease*
  - Subgenus *Viannia* with 4 main species (*L. (V.) braziliensis*, *L. (V.) guyanensis*, *L. (V.) panamensis*, and *L. (V.) peruviana*)
- *New World, Visceral Disease*
  - *L. chagasi*



# Leishmaniasis is endemic in Texas

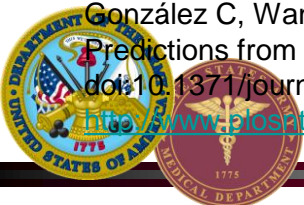


**Figure 2. Predicted current distributions for leishmaniasis vector species.**

González C, Wang O, Strutz SE, González-Salazar C, et al. (2010) Climate Change and Risk of Leishmaniasis in North America: Predictions from Ecological Niche Models of Vector and Reservoir Species. PLoS Negl Trop Dis 4(1): e585.

doi:10.1371/journal.pntd.0000585

<https://doi.org/10.1371/journal.pntd.0000585>





# What Other South American tropical disease is transmitted by sandflies ?

- Bartonellosis (Carrión's disease)
  - Also called Oroya Fever or Peruvian warts
  - Peru, Andes mountains
  - *Bartonella bacilliformis*
- Traveler infection is not common
- Fever, myalgia, headache, and anemia
- High mortality – 40%
- Chronic infection
- Rifampin, chloramphenicol  
TMP/SMX, Streptomycin

